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# Gallic acid Biological Activities: A review

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## ABSTRACT:

Phenolic acids are diverse group that includes hydroxybenzoic and hydroxycinnamic acids. Various phenolic acids reported from plants are gallic, and ellagic acids. They are also of interest in food, cosmetic and pharmaceutical industries as well as substitutes for synthetic antioxidants. One such prominent phenolic acid is gallic acid which is found in a wide variety of vegetables, fruits, tea, coffee and wine. It occurs in plants in the form of free acids, esters, catechin derivatives and hydrolysable tannins. It also occurs as methylated gallic acids e.g., syringic acid or galloyl conjugates of catechin derivatives, i.e., flanvan-3-ols, or polygalloyl esters of glucose, quinic acid or glycerol. Gallic acid has been reported to elicit various biological activities such as antibacterial, anti-fungal, antiviral, anti-inflammatory, antioxidant, anticancer, anti-diabetic effects.

**KEY WORDS:** Gallic acid, phenolic acids, plants, bioactivities

## INTRODUCTION

Medicinal plants are of great importance to health due to the presence of phytoconstituents. The most important of these constituents are alkaloids, glycosides, tannins, flavonoids, and phenolic compounds. Nature is a wealthy source of diverse and complex compounds displaying different remarkable biological effects. Phenolic acids are an important and abundant subgroup of phenolic compounds with the basic chemical structure of C6-C1 (hydroxybenzoic acids) or C6-C3 (hydroxycinnamic acids), consisting of a phenolic ring and a carboxyl substituent. Gallic acid, GA; 3, 4, 5-trihydroxy benzoic acid, is a potent natural phenolic compound present in various fruits, nuts, green tea and oak (1). Gallic acid has been reported to occur in a number of plants, some of them are Allan blackia floribunda, Garcinia densivenia, Bridelia micrantha, Caesalpinia sappan, Dillenia indica, Diospyros cinnabarina Paratecoma peroba, Psidium guajava, Syzygium cordatum, Rhus typhina, Tamarix nilotica, Vitis vinifera, Hamamelis virginiana, Toona sinensis Oenothera bienni and Rubus suavissimus (2). The structure of gallic acid has phenolic groups that are a source of readily available hydrogen atoms so that radicals produced can be delocalized over the phenolic structure (3). The interest in these compounds is due to its pharmacological activity as radical scavengers. It has been proved to have potential preventive and therapeutic effects in many diseases, where the oxidative stress has been implicated, including cardiovascular diseases, cancer, neurodegenerative disorders and in aging (4, 5). Due to these activities gallic acid could be considered as a promising lead compound for new drug development. Current review is an attempt to compile literature reporting on bioactivities on gallic acid.

## BIOLOGICAL ACTIVITIES

### Gallic Acid Inhibited Human Nasopharyngeal Carcinoma Cells

Gallic acid has been reported to inhibit the migration and invasive capability of various cancers. This study investigated the anti-invasive effect of gallic acid on human nasopharyngeal carcinoma cells (NPC-BM1) and its related mechanism. Gallic acid inhibited the invasion of NPC-BM1 cells dose- and time-dependently without significant cytotoxic effect. Affymetrix oligonucleotide microarray analysis revealed matrix metalloproteinase-1 (MMP-1) as the most down-regulated gene in NPC-BM1 cells by gallic

acid. The cytosolic and secreted MMP-1 levels were both found to be inhibited by gallic acid as demonstrated by western blot analysis and ELISA respectively. These results may be useful to develop a novel chemotherapeutic agent to inhibit the metastasis of nasopharyngeal cancer (6).

**Gallic acid improves cardiac dysfunction**

Gallic acid reduces cardiac hypertrophy, dysfunction, and fibrosis induced by transverse aortic constriction (TAC) stimuli in vivo and transforming growth factor β1 (TGF-β1) in vitro. It decreases left ventricular end-diastolic and end-systolic diameter, and recovers the reduced fractional shortening in TAC. In addition, it suppresses the expression of atrial natriuretic peptide, brain natriuretic peptide, skeletal α-actin, and β-myosin heavy chain. Administration of gallic acid decreases perivascular fibrosis, as determined by Trichrome II Blue staining, and reduces the expression of collagen type I and connective tissue growth factor. These results suggest that gallic acid is a therapeutic agent for cardiac dysfunction and fibrosis in chronic heart failure (7).

**Antimicrobial activity**

Gallic acid can inhibit motility, adherence and biofilm formation of Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus mutans, Chromobacterium violaceum, and Listeria monocytogenes (8). The compound can also disrupt the integrity of the cell membrane in Gram-positive and Gram-negative bacteria and change the charge, hydrophobicity, and permeability of the membrane surface. Gallic acid can interfere with the membrane permeability of Campylobacter jejuni and elevate the antibiotic accumulation in the microorganism (9).

**Neuropsychological diseases**

The protective effect of gallic acid on nerve cells is a controversial issue. On the one hand, gallic acid decreases the Aβ-induced toxicity in cultured cortical neurons of rats via inhibiting Ca2+ release from the endoplasmic reticulum into the cytoplasm or Ca2+ influx, inhibiting ROS generation and apoptosis (10). The compound restores the streptozotocin (STZ)-induced cerebellar oxidative stress and cognitive impairment in rats by scavenging free radical molecules such as ROS, inhibiting lipid peroxidation, and stimulating the activity of endogenous antioxidant agents, such as SOD, CAT, and GPx (11). Gallic acid is also able to reverse the scopolamine-induced amnesia in mice, probably through inhibiting oxidative stress and decreasing acetylcholinesterase (AChE) enzyme activity in the brain (12).

**Anticancer activity**

Gallic acid can exert its cytotoxic and antitumor effect via modulation of antioxidant/pro-oxidant balance. In some cases, the compound can control the reactive oxygen species (ROS)-induced carcinogenesis through increasing the activity of superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), and glutathione peroxidase (GPx) and/or by reducing the lipid peroxidation and ROS production. In other cases, gallic acid can induce the cell cycle arrest, autophagy, and apoptosis via activating the caspases pathway and ROS generation. In addition, it can inhibit the invasion and metastasis by decreasing the matrix metalloproteinase expression and activity (13).

**Metabolic diseases**

Obesity, diabetes mellitus, and hyperlipidemia are the most prevalent metabolic disorders among adults. The ability to store the excess energy in adipocytes and release it in the future is vital for survival. However, genetic susceptibility, excessive energy intake and sedentary lifestyle may provoke increased adipose storage and further cause metabolic disorders. In metabolic disorders, gallic acid inhibits diet-induced hyperglycemia and hypertriglyceridemia, reduces the size of adipocytes, and protects pancreatic β-cells by inducing the expression of peroxisome proliferator-activated receptor-γ (PPAR-γ), a nuclear transcription factor that induces differentiation and insulin sensitivity in adipocytes (Gandhi et al., 2014). Gallic acid also increases the cellular glucose uptake via stimulation of the phosphatidylinositol 3-kinase (PI3K)/p-Akt signaling pathway and translocation of insulin-stimulated glucose transporters, such as GLUT4, GLUT2, and GLUT1 (14). It prevents the diet-induced oxidative stress by stimulating various enzymatic and non-enzymatic antioxidant defenses (15). Gallic acid can up-regulate the hepatic glycolysis enzymes, such as hexokinase, aldolase, and phosphofructokinase, and down-regulate the hepatic gluconeogenesis enzyme, named fructose-1,6-bisphosphatase, in rodents fed a high fructose diet (16,17).

**Gastrointestinal diseases**

Gallic acid protects the mucosal layer of the gastrointestinal tract from ulcer via different mechanisms by reducing the acid secretion, inducing the release of

endogenous antioxidant agents and defensive factors, as well as decreasing oxidative stress and lipid peroxidation (18, 19).

**Cardiovascular diseases**

Myocardial ischemia is defined as a condition that is caused by an imbalance between oxygen supply and demand of the myocardium, of which coronary artery atherosclerosis is known to be the main cause. To decrease the risk of myocardial infarction, the ischemia can be treated using different surgical methods and/or pharmacological agents. Gallic acid pretreatment decreases the harmful oxidative consequences of myocardial infarction in the context of its antioxidant potency, either by increasing the activity of antioxidant enzymes, such as SOD, CAT, GST, and GPx and/or by elevation of the level of non-enzymatic antioxidant agents, such as GSH, vitamin C, and vitamin E (20).

## CONCLUSION

This review showed that the most important pharmacological properties of gallic acid are attributed to its antioxidant and anti-inflammatory potentials. In addition, gallic acid is involved in various signaling pathways that regulate the wide range of biological functions including inflammatory pathways, NO signaling pathway, intrinsic and extrinsic pathways of apoptosis, and NF-κB signaling pathway. Gallic acid and its derivatives demonstrated a broad range of beneficial effects in prevention and/or management of several disorders.

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